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Note

Alumina-catalysed derivatisation of sesquiterpene lactones†

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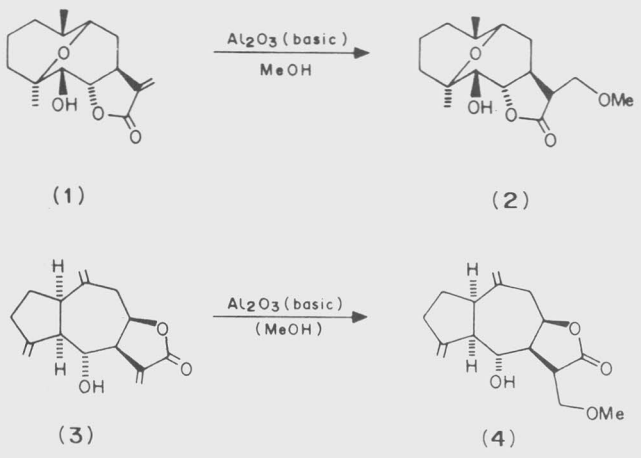
Two new derivatives **2** and **4** have been obtained by the alumina-catalysed reaction of methanol with sesquiterpene lactones **1** and **3** previously isolated from *Cyathocline* species. The structures of **2** and **4** have been elucidated by extensive NMR studies.



Many heterogenous organic reactions effected by reagents immobilised on porous solid supports like alumina have been reported[1]. These include reactions such as addition, reduction, oxidation, substitution, elimination, abstraction of acidic hydrogen, decarboxylation and skeleton rerrangements. Although Michael type addition of methanol to the methylene group of α-methylene-γ-lactone[2] and to the double bond of α, β-unsaturated ketone[3,4] and addition of water and methanol to the above systems catalysed by alumina is known[5]. During the chemical investigation of the acetone extract of *Cyathocline lutea* and *Cyathocline purpurea* we have isolated the sesquiterpene lactones **1** and **3** in major quantities[6,7]. In the present study we have converted these two compounds into 11,13-dihydro-13-methoxy derivatives (**2** and **4**) by treating with basic alumina. Sesquiterpenes having 11,13-dihydro-13-methoxy group are very rare in nature. Such a type of sesquiterpene lactone has been reported for the first time from *Sphaeranthus indicus*[8]. The alumina-catalysed products of **1** and **3** were purified by preparative TLC with acetone petrol (40:60) as eluent.

Compound 2: Viscous liquid, molecular formula $C_{16}H_{26}O_5$, showed characteristic absorption bands in its IR spectrum (3420, 1775 cm^{-1}) and signals in its ^1H NMR spectrum at δ 3.70 (dd, 1H), 3.60 (dd, 1H) and 3.40 (s, 3H) for the presence of 11,13-dihydro-13-methoxy grouping in the lactone ring. The presence of secondary and tertiary methyl was evident from a doublet at δ 0.90 and singlet at 1.20. Further, the C-6 proton appeared as a double doublet at δ 4.16 and the signal at δ 4.12 as a doublet suggested the position of lactone ring and a secondary hydroxy group. The structure and stereochemistry of compound **2** were determined by the spectral methods and critical comparison with reported spectral data of compound **1** (cf. Table I).

Compound 4: Gummy liquid, molecular formula $C_{16}H_{22}O_4$ (M^+278). Its IR spectrum showed characteristic bands at 3390 (hydroxyl group), 1770 (saturated-γ-lactone moiety) and 1660 cm^{-1} (unsaturation). The ^1H NMR spectrum showing the doublets at δ3.50 and 3.57 for one proton each and the singlet at δ3.42 (3H) clearly indicated the presence of 11,13-dihydro-13-methoxy grouping in compound **4**. The presence of two exocyclic methylene groups was indicated by broad singlets at δ 4.97 for C-14 and at 5.05 and 5.30 for C-15. The ^1H NMR spectrum further showed the appearance of H-6, H-7 and H-8 at δ 3.95(dd), 3.10(m) and 4.50(ddd). The structure was further supported by the ^{13}C NMR signals at δ 76.4(d), 58.2(d) and 77.6(d).

Assignments of the protons were achieved by ^1H-^1H-homonuclear decoupling (Figure 1) and all

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Table 1—^{1}H NMR ($CDCl_3$) data of compounds **1-4** (*J* values in Hz are given in parentheses)

Proton	1	2	3	4	Proton	1	2	3	4
H-1	—	—	2.50 m	2.47 m	H-9	3.70 m	3.80	—	—
H-2α	—	—	1.60m	1.65 m	H-11	—	2.45 m	—	—
H-2β	—	—	1.85m	1.75 m	H-13a	5.41d	3.60 dd	6.35 br..s	3.50 dd
H-3	—	—	2.30 m	2.35 m		(3.0)	(9.5,3.0)		(9.5,2.0)
H-5	4.12 d	4.12 d	2.35 m	2.38 m	H-13b	6.13 d	3.70 dd	4.95 br. s	3.57 dd
	(9.5)	(9.5)				(3.2)	(9.5, 3.0)		(9.5, 2.0)
H-6	4.15 dd	4.16 dd	3.75 dd	3.95 dd	H-14	0.88d	0.90d	5.00 br..s	4.97 br..s
	(9.5,9.5)	(9.5,9.5)	(10.0,10.0)	(10.0,10.0)		(6.8)	(6.8)		
H-7	2.5m	2.65m	3.20	3.10m	H-15a	1.20 s	1.20 s	5.05 br.s	5.05 br.s
H-8	—	—	4.4 ddd	4.50 ddd	H-15b	—	—	5.10 br.s	5.30 br.s
			(9.0,11.0,4.0)	(9.0,11.0,4.0)	OMe	—	3.40 s	—	3.42 s

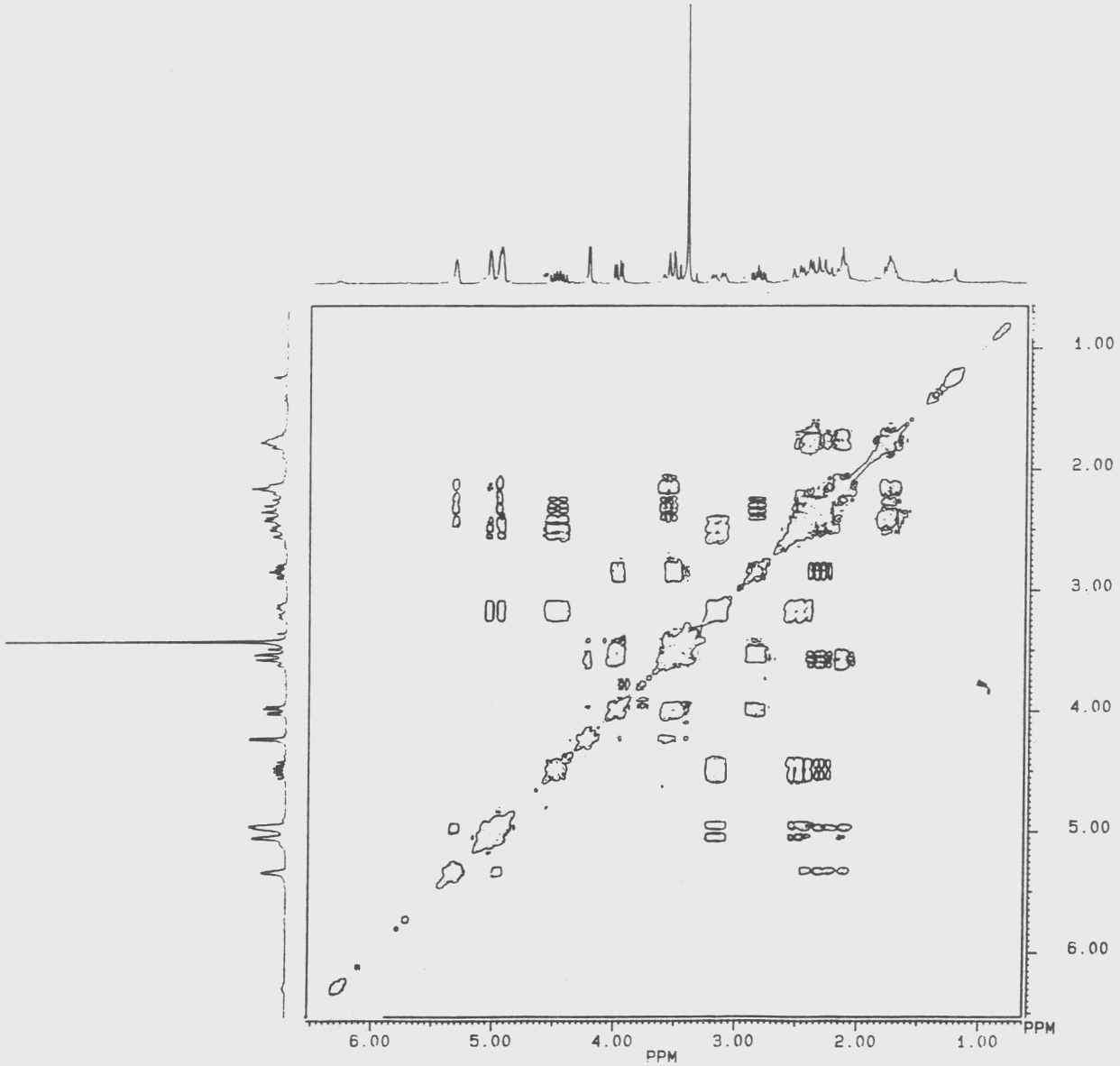

Figure 1—^{1}H-^{1}H-homonuclear decoupling spectrum of compound **4**.

multiplicities in the ^{13}C NMR were determined by INEPT technique. On the basis of above evidence we assigned the structure and stereochemistry to compound **4**.

Experimental Section

Compound **1** was isolated from the acetone extract of *Cyathocline lutea* by repeated column chromatography and preparative TLC using the solvent systems EtOAC-benzene (30:70) and Me_2CO-petrol (40:60).

Compound **3** was isolated from the acetone extract of the aerial parts of *Cyathocline purpurea* by repeated column chromatography coupled with preparative TLC using different solvent systems.

Methoxylation of 1. Compound **1** (200 mg) dissolved in methanol (200 mL) was refluxed with 25 g of basic alumina for 24 hr. usual work-up gave the compound **2** (135 mg) as a viscous liquid; IR:3420, 1775, cm^{-1}, ^1H NMR($CDCl_3$): Table 1; MS:m/z 298$(M)^+$ (5%), 280(2), 253(11), 241(9), 159(27), 121(32), 95(42), 81(52), 71(56) and 55(100).

Methoxylation of 3. Compound **3** (500 mg) dissolved in methanol (500 mL) was refluxed with 75 g of basic alumina for 24 hr. Usual work-up gave the compound **4** (275 mg) as a gummy liquid; IR($CHCl_3$):3390, 1770 and 1660 cm^{-1}; ^1H NMR ($CDCl_3$); Table 1; ^{13}C NMR ($CDCl_3$): δ 45.0 (t, C-1), 29.7(t, C-2), 32.9 (t, C-3), 144.8 (s, C-4), 48.8 (d, C-5), 76.4 (d, C-6), 58.2 (d, C-7), 77.6 (d, C-8), 40.5 (t, C-9), 152.2 (s, C-10), 53.2 (d, C-11), 174.3 (s, C-12), 71.5 (t, C-13), 108.5 (t, C-14), 112.2 (t, C-15), 59.2 (q, OMe); MS: m/z 278(M^+) (2%), 207(10), 121(42), 117(10), 107(22), 91(32), 79(20), 69(18) and 55(15).

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